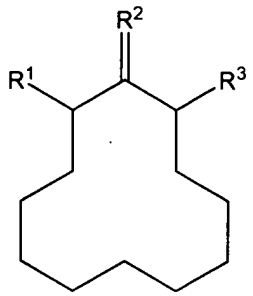
CLAIMS

What is claimed is:

1. A method of inhibiting function and/or proliferation of a cell expressing Janus tyrosine kinase 3 comprising contacting the cell with at least one compound of the formula (I)



wherein

R^1 is H, $=CH_2$, $CH_2N(CH_3)_2$, $CH_2SC(O)CH_3$, $CH_2SC_6H_5$, CH_2SCH_2-(4-$C_6H_4OCH_3$), $CH_2SC(O)C_6H_5$ or $CH_2N(CH_2CH_3)_2$;

R^2 is O;

R^3 is $CH_2N(CH_3)_2$, $CH_2N(CH_2CH_3)_2$ or CH_2-(N-morphyl);

or a salt thereof, at a concentration effective to selectively inhibit Janus tyrosine kinase 3 activity.

2. The method of claim 1 wherein R^1 is $CH_2N(CH_3)_2$ and R^3 is $CH_2N(CH_3)_2$.

3. The method of claim 2 wherein said compound is the meso stereoisomer.

4. The method of claim 1 wherein the cell is of lymphoid or myeloid origin.

5. The method of claim 1 comprising interfering with the signal 3 pathway in said cell such that cell division is blocked.

6. The method of claim 1 wherein, at said concentration effective to selectively inhibit said Janus tyrosine kinase 3, said at least one compound is substantially non-inhibitory of protein tyrosine kinase activity other than Janus tyrosine kinase 3 activity.

7. The method of claim 1 wherein said cell is a T-cell, and the method comprises inhibiting Jak3 activity at least 3 fold more than inhibiting Jak2 activity in said T-cells.

8. The method of claim 1 comprising choosing at least one said compound which is less capable of inhibiting Jak2 and Stat5a/b activation by prolactin (PRL) at a concentration sufficient to inhibit Jak3 and Stat5a/b activated by IL2.

9. An *in vitro* testing method to aid in identifying substances that are useful as therapeutic immunosuppressants, the method comprising:

(a) obtaining a population of quiescent Jak3 dependent T lymphocytes in cell culture medium;

(b) optionally, pretreating the quiescent T lymphocytes with a cytokine to stimulate said lymphocytes to proliferate;

(c) treating said quiescent or stimulated lymphocytes from step (a) or (b) with a compound, or salt thereof, as defined in claim 1;

(d) culturing the lymphocytes from step (c) under cell growth promoting conditions;

(e) assessing the extent of cell proliferation following step (d);

(f) optionally, assessing the inhibitory effect of said compound on Jak2-dependent T lymphocyte proliferation;

(g) optionally, assessing cytotoxicity of said compound;

(h) determining from the assessments from step (e) and from (f) and (g), if present, that significant inhibition of Jak3-dependent lymphocyte proliferation, not attributable to cytotoxicity of the compound, suggests that the compound has potential as a candidate drug for therapeutic use *in vivo* as a T-cell mediated immunosuppressant and/or as an inhibitor of T-cell proliferation; and

(i) optionally, comparing the assessments from steps (e) and (f), and, if the inhibitory effects assessed in step (f) are significantly less than the inhibitory effects assessed in step (e), determining from said comparison that said compound is selective to at least some extent for inhibiting Jak3 activity compared to inhibiting Jak2 activity.

10. An *in vivo* method of suppressing an undesired function of a cell expressing Janus tyrosine kinase 3 in a mammalian subject in need thereof comprising:

contacting said cell with at least one compound as defined in claim 1, or a metabolite or derivative thereof, in an amount effective to interfere with the signal 3 pathway in the cell and thereby inhibit cell function,

said contacting comprising administering to said subject a therapeutically effective amount of a pharmaceutical composition containing at least one said compound, as defined in claim 1, or pharmaceutically acceptable salt thereof, or a metabolite of said compound, or a precursor of said

compound capable of being converted in the body of the subject to said compound, in a pharmaceutically acceptable carrier, to inhibit Jak3-dependent cell function.

11. The method of claim 10 wherein said cell is a T-cell and said amount of said pharmaceutical composition is effective to block cell division in said T-cell.

12. The method of claim 10 comprising continuously or periodically administering said pharmaceutical composition to the subject

13. A method of therapeutically treating a mammalian subject to suppress an undesired immune response comprising carrying out the method of claim 10 wherein said subject is experiencing or is at risk of experiencing an undesired immune response, and said therapeutically effective amount of said pharmaceutical composition mitigates or prevents said undesired immune response.

14. The method of claim 13 further comprising administering to said subject a therapeutically effective amount of an immunosuppressive agent other than a Jak3 inhibitor.

15. The method of claim 14 wherein said other immunosuppressive agent is cyclosporin A or FK506.

16. A method of mitigating organ transplant rejection in a mammalian transplant recipient comprising carrying out the method of claim 10 to suppress a T-cell mediated immune response to the transplanted organ whereby rejection of the organ is mitigated or arrested.

17. A method of mitigating acute allograft rejection in a mammalian allograft recipient comprising carrying out the method of claim 10 to suppress a T-cell mediated anti-allograft immune response to said allograft whereby acute rejection of the allograft is mitigated or prevented.

18. A method of inducing transplantation tolerance in a mammalian transplant recipient comprising carrying out the method of claim 10 to suppress a T-cell mediated transplant rejection response.

19. A method of promoting remission of an autoimmune disease in a mammalian subject suffering from said disease comprising carrying out the method of claim 10 to suppress a T-cell mediated autoimmune response in said subject whereby autoimmune attack on the subject's native tissue mediated by endogenous Jak3-dependent T-cells is diminished or arrested.

20. A method of mitigating airway hypersensitivity in a mammalian subject suffering from said hypersensitivity comprising carrying out the method of claim 10 to suppress a T-cell mediated hypersensitivity response in said subject whereby hypersensitivity of airway tissue in said subject is diminished or arrested.

21. A method of mitigating allergy in a mammalian subject suffering from said allergy comprising carrying out the method of claim 10 to suppress a T-cell mediated allergic response in said subject whereby an allergic reaction in said subject is diminished or arrested.

22. A method of inhibiting proliferation of a Jak3-dependent leukemia or lymphoma comprising carrying out the method of claim 10, wherein said subject suffers from leukemia or lymphoma, wherein said compound or said metabolite is capable of selectively inhibiting Jak3 activity compared to other kinase activity, to inhibit or block proliferation of leukemia or lymphoma cells.

23. The method of claim 10 wherein nephrotoxicity of said compound is less than that of cyclosporin A.

24. The method of claim 10 further comprising administering another immunosuppressive agent.

25. An *in vitro* method to aid in identifying a new immunosuppressive drug comprising:

testing a compound of interest for activity for disrupting T-cell function by contacting a T-cell comprising Jak3 with said compound of interest over a range of concentrations and determining whether said compound inhibits Jak3 activity at one or more concentration within said range;

comparing the Jak3 inhibitory activity of said compound of interest to that of the compound as defined in claim 2 having known Jak3 inhibitory activity; and

using the results of said testing and comparing to determine whether said compound of interest is a candidate drug for *in vivo* use as a therapeutic immunosuppressive agent.

26. The method of claim 25 further comprising:

testing said compound of interest for Jak2 inhibitory activity;

comparing the Jak3 inhibitory activity of said compound of interest to its Jak2 inhibitory activity, if any; and

using said comparison to identify said compound of interest as a selective Jak3 inhibitor.

27. An *in vivo* method of testing a candidate immunosuppressive drug for its effect on allograft survival comprising:

(a) implanting an allograft taken from a suitable donor animal into a suitable recipient animal;

(b) maintaining basic nutrition and health promoting conditions for the animals;

(c) administering the candidate drug to each of at least one animal, to provide a treated recipient or group;

(d) administering to at least one animal the compound as defined in claim 1, wherein R^1 and R^3 are each $CN(CH_3)_2$ and R^2 is O, to serve as a positive control group;

(e) optionally, leaving at least one recipient animal untreated, to serve as an untreated control recipient or group;

(f) determining allograft survival time of each allograft in each recipient;

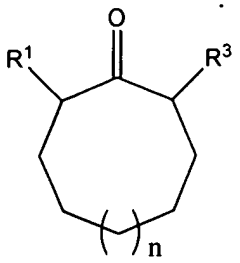
(g) performing histological examination of each allograft and assessing candidate drug related structural damage to each allograft, as applicable;

(h) comparing the allograft survival time and the candidate drug induced histological structural changes in each allograft; and

(i) using the comparisons from (h), determining that enhanced graft survival time and lack of drug induced structural damage to the drug treated allografts compared to the allograft(s) from the untreated control recipient(s) or compared to the allograft(s) from the positive control recipient(s) is indicative that the candidate drug is likely to be effective when used therapeutically *in vivo* as an immunosuppressive agent.

28. The method of claim 27 comprising determining that said candidate drug is capable of selectively inhibiting Jak3 dependent T-cell proliferation *in vitro.*

29. A method of inhibiting function and/or proliferation of a cell expressing Janus tyrosine kinase 3 comprising contacting the cell with at least one compound of the formula (II)



wherein

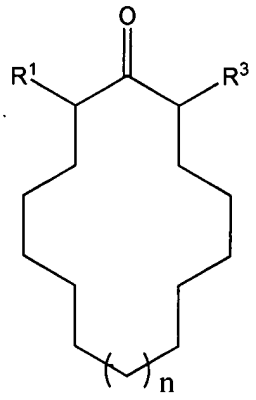
n is 1,2,3,4 or 6;

R^1 is H, CH_2, or $CH_2N(CH_3)_2$;

R^3 is $CH_2N(CH_3)_2$;

or a salt thereof, at a concentration effective to selectively inhibit the activity of said Janus tyrosine kinase 3.

30. A method of inhibiting function and/or proliferation of a cell expressing Janus tyrosine kinase 3 comprising contacting the cell with at least one compound of the formula (III)



wherein

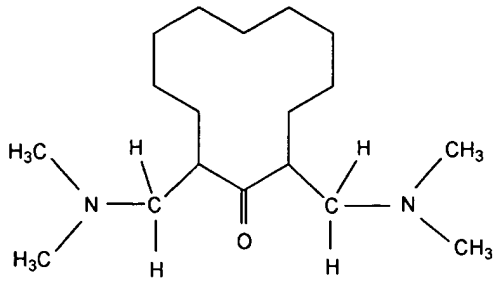
n is 1 or 2;

R^1 is H, or $CH_2N(CH_3)_2$;

R^3 is $CH_2N(CH_3)_2$;

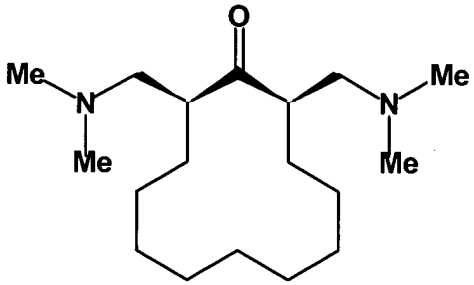
or a salt thereof, at a concentration effective to selectively inhibit the activity of said Janus tyrosine kinase 3.

31. A method of inhibiting function and/or proliferation of a cell expressing Janus tyrosine kinase 3 comprising contacting the cell with at least one compound of the formula



or a salt thereof, at a concentration effective to selectively inhibit the activity of said Janus tyrosine kinase 3.

32. An isolated or purified chemical compound having the formula



or a salt thereof.

33. A pharmaceutical composition comprising the compound of claim 32, or a pharmaceutically acceptable salt thereof, in a carrier.